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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1623	

NOTIFICATION DATE	DELIVERY MODE
11/26/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/764,989	BUHLER ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 Aug 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-46* is/are pending in the application.

4a) Of the above claim(s) *18-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-17 and 30-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 08 Aug 2008, in which claims 1, 9, 10, 11, 13, 30 and 40 are amended to change the scope and breadth of the claim and claims 3, 4, 5, 14, 16, 43 and 45 are amended to correct minor informalities.

This application is a domestic application, filed 26 Jan 2004; and claims benefit of provisional application 60/449,070, filed 21 Feb 2003.

Claims 1 and 3-46 are pending in the current application. Claims 18-29, drawn to non-elected inventions, are withdrawn. Claims 1, 3-17 and 30-46 are examined on the merits herein.

Rejections Withdrawn

Applicant's Amendment, filed 08 Aug 2008, with respect to claims 1, 3-17 and 30-46 rejected under 35 U.S.C. 112, second paragraph as being indefinite has been fully considered and is persuasive, as amended claims 1 and 30 do not recite "a compound comprising" or "the photolabile protective group", and amended claims 8-11 do not recite "protective group".

This rejection has been **withdrawn**.

The following modified grounds of rejection are necessitated by Applicant's Amendment, filed 08 Aug 2008, in which claims 1, 9, 10, 11, 13, 30 and 40 are

amended to change the scope and breadth of the claim and claims 3, 4, 5, 14, 16, 43 and 45 are amended to correct minor informalities. Claims 3-17 depend directly or indirectly from claim 1 and incorporate all limitations therein, including changes in the scope and breadth of the claim. Claims 31-46 depend from claim 30 and incorporate all limitations therein, including changes in the scope and breadth of the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 1, 3-17 and 30-46 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had full possession of the claimed invention. Claims 1, 3-17 and 30-46 recite the terms “substituted,” “leaving group,” “photolabile protective group,” “functional group useful in oligonucleotide synthesis,” “protective group useful in oligonucleotide synthesis,” “chemical modifications thereof," “chemically modified," and “analog” used to describe a chemical compound.

The specification discloses chemicals, such as aryl groups "substituted" with an alkyl group (page 11, line 20), "leaving groups” such as imidazolyl (page 12, line 16), and “analogs” or "chemically modified” compounds such as 5-position pyrimidine modifications (page 12, line 20), and fully described compounds such as disclosed on

table 1 of page 53, which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 1, 3-17 and 30-46 are directed to encompass compounds described by the terms “substituted,” “leaving group,” “photolabile protective group,” “functional group useful in oligonucleotide synthesis,” “protective group useful in oligonucleotide synthesis,” “chemical modifications thereof," “chemically modified," and “analog”, which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these compounds meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and because chemical compounds are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claims. Exemplary definitions are provided for the terms, for example spanning pages 11-13, however no limiting definition is provided for these terms. Applicant’s remarks, filed 15 Dec 2006, page 30 recite “As such, it is therefore neither possible nor necessary to list explicitly all theoretically conceivable “leaving groups.”", emphasis added, as the scope of the claimed genus is so broad that simply listing it is not possible.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the structurally defined chemical compounds, but not the full breadth of the claims, meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear

that the written description provision of 35 USC § 112 is severable from its enablement provision. (See Vas-Cath at page 1115.)

The court of *In re Curtis* held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when… the evidence indicates ordinary artisans could not predict the operability … of any other species." (see *In re Curtis* 354 F.3d 1347, 69 USPQ2d 1274, Fed. Cir. 2004). The court of *Noelle v. Lederman* also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, and no description of human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown" failed. See 355 F.3d 1343, 69 USPQ2d 1508, Fed. Cir. 2004.

Therefore, because the genus of compounds encompassed by compounds described using the terms "substituted," "leaving group," "photolabile protective group," "functional group useful in oligonucleotide synthesis," "protective group useful in oligonucleotide synthesis," "chemical modifications thereof," "chemically modified," and "analog", the specification provides insufficient written description to support the genus that is being claimed.

Response to Applicant's Remarks:

Applicant's Remarks, filed 08 Aug 2008, have been fully considered and not found to be persuasive.

It is reiterated that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See Vas-Cath at page 1115.)

Applicant remarks that “a functional group useful in oligonucleotide synthesis,” “protective group useful in oligonucleotide synthesis,” “chemically modified," and “analog thereof ,” “chemical modifications thereof," and "analogs of deoxyribonucleosides, ribonucloesides, deoxyribonucleosides, and ribonucleotides” are well known and have an art recognized meaning. Applicant helpfully identifies citations within Pfleiderer et al. where the language "a functional group useful in oligonucleotide synthesis", "chemically modified", "analog thereof', and "chemical modifications thereof” are used. The citations within Pfleiderer et al. also indicate examples of structural features for said language.

However, that a genus is used in the art does not every species of that genus is known. The species specifically disclosed are not representative of the genus of the term because the genus is highly variant. Therefore the species disclosed, and not the full breadth of the claims, meet the written description provision of 35 USC § 112, first paragraph. It is noted that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*. Adequate written description requires more than a mere statement that it is part of the invention and non-limiting examples of the genus that are not representative of the fully scope of the genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended claims 1, 3-17 and 30-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1, from which claims 3-17 depend, recites "substituted" in reference to alkyl, alkoxy, aryl, and aroyl heteroaryl groups. Claims 3 and 4 additionally recites "substituted" in reference to phenyl and benzyl. The specification does not clearly define or point out what type of groups will be used in substitution and in what positions the substitutions will occur. As such, said recitation renders the claims indefinite. Claim 30, from which claims 31-46 depend, recites "substituted" in reference to alkyl, alkoxy, aryl, and aroyl heteroaryl groups.

Regarding amended claim 13, the claim recites the phrase "OH-protective group". Said phrase does not convey a structural formula or chemical name to one of ordinary skill in the art. In the absence of a structural formula or chemical name one of ordinary skill in the art would not be apprised of the metes and bounds of claimed invention so as to understand how to avoid infringement.

As indicated in the previous office action, the phrases "a functional group useful in oligonucleotide synthesis", "chemically modified", "analog thereof', and "chemical modifications thereof' does not convey any structural features to one of skill in the art. Applicants argue that "analogs of deoxyribonucleosides, ribonucloesides, deoxyribonucleosides, and ribonucleotides are well-known in the art." Applicants argue

that there might be some compounds that might be some examples in the art of analogs. However, definition by exemplification does not convey to one of skill in the art the metes and bounds of the claimed invention so as to understand how to avoid infringement. In regards to the phrase "chemically modified", the applicants points to definitions section in specification, Page 12, lines 22-page 13, line 11". The referred sections of the specification is a definition for "oligonucleotide", in which the term "oligonucleotide" is defined to include chemical modifications. The specification states that, "Modifications include, but are not limited to" a list of chemical reactions. There are no limiting definitions in the specification. Since the chemical modifications are only exemplified, and one of skill in the art will not readily know which reactions are included and which are excluded, the metes and bounds of the claims herein are not clearly defined so as to understand how to avoid infringement. The phrase "a functional group useful in oligonucleotide synthesis" is also not clearly defined so that one of skill in the art will be apprised of the metes and bounds of the claimed invention herein so as to understand how to avoid infringement. For the above reasons claims 1 and 3-17 and 30-46 are considered properly rejected under 35 USC 112 second paragraph, in regards to phrases, "a functional group useful in oligonucleotide synthesis", "chemically modified", "analog thereof', and "chemical modifications thereof."

Response to Applicant's Remarks:

Applicant's Remarks, filed 08 Aug 2008, have been fully considered and not found to be persuasive.

MPEP 2173.02 provides guidance: “The essential inquiry pertaining to this requirement [for definiteness of 35 U.S.C. 112, second paragraph] is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.”

Applicant helpfully identifies citations within Pfleiderer et al. where the language "a functional group useful in oligonucleotide synthesis", "chemically modified", "analog thereof', and "chemical modifications thereof” are used. One possessing the ordinary level of skill in the pertinent art at the time the invention was made would not find the claims insolubly ambiguous without a discernible meaning after all reasonable attempts at construction. However, MPEP 2173.02 also provides “If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate.” The citations within Pfleiderer et al. also indicate examples of structural features for said language. As recited above, definition by exemplification does not convey to one of skill in the art the metes and bounds of the claimed invention so as to understand how to avoid infringement. One possessing the ordinary level of skill in the pertinent art at the time

the invention was made would understand the examples identified are encompassed within the language, but absent a definition of what structural features are required by said language, one of ordinary skill in the art would not know the metes and bounds of the claim with clarity and precision sufficient so as to understand how to avoid infringement.

Claim Rejections - 35 USC § 103

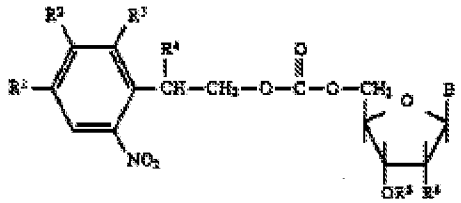
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended claims 1, 3, 5 and 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pfleiderer et al. (US Patent 5,763,599, issued 09 Jun 1998, of record) and Fodor et al. (US Patent 5,489,678, issued 06 Feb 1996, cited in PTO-892).

Pfleiderer et al. discloses compounds of the formula

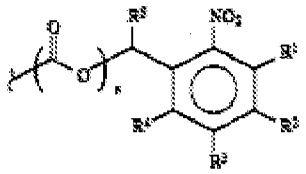


(numbering the same as the instant formula) in which R1 = H, NO2, CN, OCH3, halogen or alkyl or alkoxyalkyl having 1 to 4 C atoms; R2 = H, OCH3; R3 = H, F, Cl, Br, NO2; R4 = H, halogen, OCH3, or an alkyl radical having 1 to 4 C atoms; R5 = H or a usual functional group for preparing oligonucleotides; R6 = H, OH, halogen or XR8, where X = O or S and R8 represents a protective group usual in nucleotide chemistry; and B = adenine, cytosine, guanine, thymine, uracil, 2,6-diaminopurin-9-yl, hypoxanthin-9-yl, 5-methylcytosin-1-yl, 5-amino-4-imidazolcarboxamid-1-yl, or 5-amino-4-imidazolcarboxamid-3-yl, where in the case of B=adenine, cytosine or guanine, the primary amino function optionally exhibits a permanent protective group (abstract). Pfleiderer et al. discloses compounds with phosphoramidite substituents at the R5 position (Claim 1, Column 28; lines 37-67 Column 24-25, Summary of the Preparation Examples, Compounds 15-17). The substituents at the R3 and R4 position are identically disclosed as the instant application. (Column 28, lines 50-60; Claim 1). The substituents R5 and R6 have significant overap with the instant application. (Column 28, lines 57-67; Claim 1). Pfleiderer et al. discloses substitution of Sulfur and Oxygen at the R6 position as well as

the use of protecting groups including silyl groups for oxygen. In particular, alkyl, alkenyl, acetal, S-alkyl, O-Methyl, O-ethyl, O-alkenyl O-allyl, O-acetal and O-tetrahydropyranyl groups are disclosed. (Column 28, lines 37-67, Claim 1; Column 2, lines 52-65). Pfleiderer et al. discloses the use of the bases adenine, cytosine and guanine, and the protective groups p-NPEOC and ethylformamidino. (Column 29, lines 30-40, claims 10,11 and 13).

Pfleiderer et al. does not specifically disclose compounds wherein R2 is selected from the group consisting of an optionally substituted aryl group, an optionally substituted heteroaryl group or an optionally substituted aroyl group.

Fordor et al. teaches photolabile nucleoside protecting groups of the formula



where R1, R2, **R3** (corresponding to R2 of the instant formula), and R4 independently are a hydrogen atom, a lower alkyl, **aryl**, benzyl, halogen, hydroxyl, alkoxyl, thiol, thioether, amino, nitro, carboxyl, formate, formamido or phosphido group, or adjacent substituents (i.e., R1 -R2, R2 -R3, R3 -R4) are substituted oxygen groups that together form a cyclic acetal or ketal (column 19, lines 50-67). Fordor et al. teaches "The removal rate of the protecting groups depends on the wavelength and intensity of the incident radiation, as well as the physical and chemical properties of the protecting group itself. Preferred protecting groups are removed at a faster rate and with a lower intensity of radiation. For example, at a given set of conditions, MeNVOC and MeNPOC are photolytically removed from the N-terminus of a

peptide chain faster than their unsubstituted parent compounds, NVOC and NPOC, respectively." (column 24, lines 45-57) Fordor et al. provides guidance for varying the substituents R1, R2, R3, and R4 because varying the substituents results in protecting groups that are removed at a faster rate (column 25, table in lines 30-40).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the compound disclosed by Pfleiderer et al. with the teaching of Fordor et al. of varying the substituents of the phenyl ring. Both Pfleiderer et al. and Fordor et al. are directed to the field of photolabile protecting groups of nucleosides. Fordor et al. provides guidance for varying the substituents R1, R2, R3, and R4 because varying the substituents results in protecting groups that are removed at a faster rate and teaches “Preferred protecting groups are removed at a faster rate and with a lower intensity of radiation”. Therefore it would have been obvious to try, selecting from a finite number of identified, predictable solutions, with a reasonable expectation of success to practice the compound wherein R2 is selected from the group consisting of an optionally substituted aryl group.

Response to Applicant's Remarks:

Applicant’s Remarks, filed 08 Aug 2008, have been fully considered and not found to be persuasive.

Applicant remarks that the Fodor et al. patent is drawn to a photolabile compound of a significantly different structure than the instantly claimed compound. However, the teaching of Fodor et al. relied upon is drawn to the guidance for varying the substituents R1, R2, R3, and R4 of the nitrophenyl ring because varying the

substituents results in protecting groups that are removed at a faster rate and teaches "Preferred protecting groups are removed at a faster rate and with a lower intensity of radiation". It is well known in the art that it is the aromatic ring that absorbs near-UV and visible radiation (Fodor et al. column 19, lines 43-50). This aromatic ring is common to the inventions of Pfleiderer et al. and Fodor et al., in the same field of photolabile protecting groups of nucleosides. Fodor et al. does not specifically teach the preferred embodiment wherein **R3** of Fodor et al. (corresponding to R2 of the instant formula) is aryl, but does provide guidance to vary the substituent to be aryl. Therefore it would have been obvious to try, selecting from a finite number of identified, predictable solutions, with a reasonable expectation of success

Applicant remarks that Fodor et al. teaches the compound with a photolabile benzyl group and not a phenethyl group. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The disclosure of Pfleiderer et al. of a photolabile phenethyl group combined with the teaching of Fodor et al. of varying the substituents of the photolabile aryl group renders obvious the instant invention.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

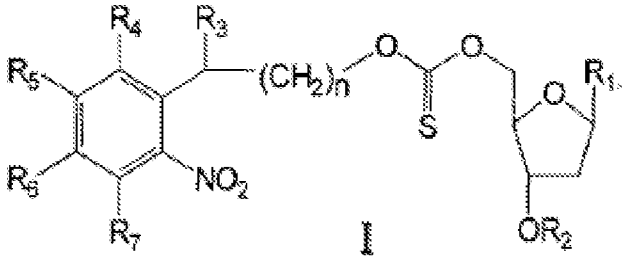
Discussion of Hasan et al. contributes to establishing a background for determining obviousness in determining the scope of the prior art and resolving the level of ordinary skill in the pertinent art, according to the inquiries set forth in *Graham* **v.** *John Deere Co.* However, the contents of Hasan et al. are not relied upon in the combination of Pfleiderer et al. in view of Fordor et al.

Amended claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pfleiderer et al. (US Patent 5,763,599, issued 09 Jun 1998, of record) and Fodor et al. (US Patent 5,489,678, issued 06 Feb 1996, cited in PTO-892) as applied to claims 1, 3-5 and 7-17 above, and further in view of Berlin (DE19938092, published 22 Feb 2001, cited in PTO-892). As DE19938092 is published in German, a machine translation of Berlin is provided.

Pfleiderer et al. and Fodor et al. teaches as above.

Pfleiderer et al. and Fodor et al. do not specifically disclose the compound wherein W is S (instant claim 6).

Berlin teaches photo-unstable protecting groups of nucleoside derivatives that that can be split off very efficiently (page 2, lines 4-5 of the machine translation; page 3 lines 39-40 of DE 19938092). Berlin teaches said protecting groups can be manufactured analogous to the esters of carbonic acid (page 2, lines 6-7 of the machine translation; page 3, lines 41-42 of DE 19938092), the compound where W is O

according to the formula of instant claim 1. Berlin teaches compounds of represented by the formula  (DE 19938092, abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the compound taught by Pfleiderer et al. and Fodor et al. with the teaching of Berlin of the compound wherein W is S according to the formula of instant claim 1. All of Pfleiderer et al., Fodor et al. and Berlin are directed to the field of photolabile protecting groups of nucleosides. One of ordinary skill in the art would be motivated to combine Pfleiderer et al. and Fodor with the teaching of Berlin because Berlin teaches use of the thiocarbonic group results in a protecting group that can be split off very efficiently. One of ordinary skill in the art would have a reasonable expectation of success in combining Pfleiderer et al. and Fodor with the teaching of Berlin because of the structural similarities of the compounds and the teaching of Berlin that said protecting groups can be manufactured analogous to the esters of carbonic acid.

Response to Applicant's Remarks:

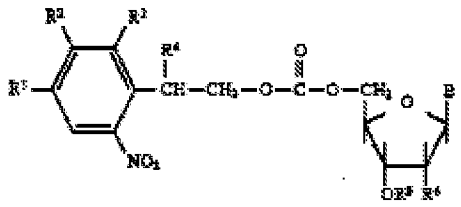
Applicant's Remarks, filed 08 Aug 2008, have been fully considered and not found to be persuasive.

The response to Applicant's remarks regarding Pfleiderer et al. and Fodor et al. is as detailed above.

Applicant remarks that Berlin teaches a compound that is has different substituents at the aryl ring of the photolabile aryl group. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The disclosure of Pfleiderer et al. of a photolabile phenethyl group combined with the teaching of Fodor et al. of varying the substituents of the photolabile aryl group and further in view of the teaching of Berlin renders obvious the instant invention.

Amended claims 30-32 and 34-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pfleiderer et al. (US Patent 5,763,599, issued 09 Jun 1998, of record) in view of Haugland et al. (US Patent 5,635,608, issued 03 Jun 1997, cited in PTO-892).

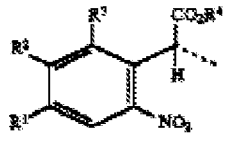
Pfleiderer et al. discloses compounds of the formula



(numbering the same as the instant formula) in which R1 = H, NO2, CN, OCH3, halogen or alkyl or alkoxyalkyl having 1 to 4 C atoms; R2 = H, OCH3; R3 = H, F, Cl, Br, NO2; R4 = H, halogen, OCH3, or an alkyl radical having 1 to 4 C atoms; R5 = H or a usual functional group for preparing oligonucleotides; R6 = H, OH, halogen or XR8, where X = O or S and R8 represents a protective group usual in nucleotide chemistry; and B = adenine, cytosine, guanine, thymine, uracil, 2,6-diaminopurin-9-yl, hypoxanthin-9-yl, 5-methylcytosin-1-yl, 5-amino-

4-imidazolcarboxamid-1-yl, or 5-amino-4-imidazolcarboxamid-3-yl, where in the case of B=adenine, cytosine or guanine, the primary amino function optionally exhibits a permanent protective group (abstract). Pfleiderer et al. discloses compounds with phosphoramidite substituents at the R5 position (Claim 1, Column 28; lines 37-67 Column 24-25, Summary of the Preparation Examples, Compounds 15-17). The substituents at the R3 and R4 position are identically disclosed as the instant application. (Column 28, lines 50-60; Claim 1). The substituents R5 and R6 have significant overap with the instant application. (Column 28, lines 57-67; Claim 1). Pfleiderer et al. discloses substitution of Sulfur and Oxygen at the R6 position as well as the use of protecting groups including silyl groups for oxygen. In particular, alkyl, alkenyl, acetal, S-alkyl, O-Methyl, O-ethyl, O-alkenyl O-allyl, O-acetal and O-tetrahydropyranyl groups are disclosed. (Column 28, lines 37-67, Claim 1; Column 2, lines 52-65). Pfleiderer et al. discloses the use of the bases adenine, cytosine and guanine, and the protective groups p-NPEOC and ethylformamidino. (Column 29, lines 30-40, claims 10,11 and 13).

Pfleiderer et al. does not specifically disclose the compound wherein R1 is COOY.

Haugland et al. teaches caged compounds with a photoremovable α-carboxy-subtituted o-nitrobenzyl group (abstract) attached to compounds such as nucleosides or nucleotides (figure 1, compounds 21 and 27 and column 4, lines 45-46) wherein the photoremovable group is represented by the formula  wherein cage

substituents R1 and R2, which may be the same or different, are H, --(C=O)--Cl, --CO_2R7, --OR8 or --O--$(CH_2)_n$--CO_2R7, where R7 is H, a linear or branched alkyl ester containing 1-6 carbons, an acetoxymethyl ester (--CH_2--O--(C=O)--CH_3), or a succinimidyl ester, or a carboxylate salt (column 3, lines 15-30). Haugland et al. teaches "The careful selection of substituent R7 can be used to modify the solubility properties of the caged product, such as for the purpose of enhancing its uptake by biological cells, or R7 substituents may permit the covalent attachment of the caged molecule to another organic molecule, such as for the purpose of targeting the caged molecule to a specific location or limiting diffusion of the caged molecule…" (column 3, lines 36-42).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the compound disclosed by Pfleiderer et al. with the teaching of Haugland et al. of varying the substituent R1 to carboxyl group. Both the inventions of Pfleiderer et al. and Haugland et al. are directed to the field of photoremovable protecting groups. One of ordinary skill in the art would be motivated to combine Pfleiderer et al. in view of Haugland et al. because Haugland et al. teaches the careful selection of substituent R7, part of the group --CO_2R7, can be used to modify the solubility properties of the caged product, such as for the purpose of enhancing its uptake by biological cells, or R7 substituents may permit the covalent attachment of the caged molecule to another organic molecule, such as for the purpose of targeting the caged molecule to a specific location or limiting diffusion of the caged molecule. One of ordinary skill in the art would have a reasonable expectation of success in combining

Pfleiderer et al. in view of Haugland et al. because both inventions are drawn to a photoremovable group with a common core, and Haugland et al. teaches "The photolytic removal of CAGE depends only on the presence of the O-nitrobenzyl moiety and a single benzylic hydrogen atom..." (spanning column 3, lines 66-67 and column 4, line 1). Therefore it would have been obvious to try, selecting from a finite number of identified, predictable solutions, with a reasonable expectation of success to practice the compound wherein R1 is the group COOY.

Response to Applicant's Remarks:

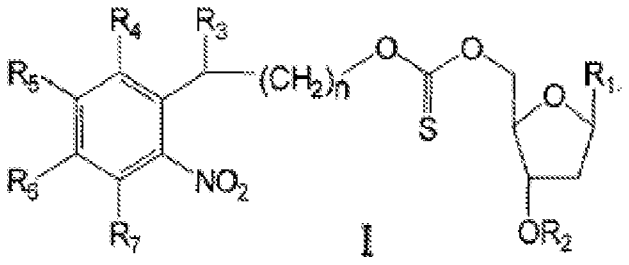
Applicant's Remarks, filed 08 Aug 2008, have been fully considered and not found to be persuasive.

Applicant remarks that Haugland et al. does not teach the instantly claimed invention because Haugland et al. teaches the compound with a photolabile benzyl group and not a phenethyl group and the compound taught by Haugland et al. encompasses the functional group at position R^1 and R^2 selected from the same group of elements. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The disclosure of Pfleiderer et al. of a photolabile phenethyl group combined with the teaching of Haugland et al. of varying the substituents of the photolabile aryl group renders obvious the instant invention.

Amended claims 30 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pfleiderer et al. (US Patent 5,763,599, issued 09 Jun 1998, of record) in view of Haugland et al. (US Patent 5,635,608, issued 03 Jun 1997, cited in PTO-892) as applied to claims 30-32 and 34-46 above, and further in view of Berlin (DE19938092, published 22 Feb 2001, cited in PTO-892). As DE19938092 is published in German, a machine translation of Berlin is provided.

Pfleiderer et al. and in view of Haugland et al. teaches as above.

Pfleiderer et al. and in view of Haugland et al. do not specifically disclose the compound wherein W is S (instant claim 33).

Berlin teaches photo-unstable protecting groups of nucleoside derivatives that that can be split off very efficiently (page 2, lines 4-5 of the machine translation; page 3 lines 39-40 of DE 19938092). Berlin teaches said protecting groups can be manufactured analogous to the esters of carbonic acid (page 2, lines 6-7 of the machine translation; page 3, lines 41-42 of DE 19938092), the compound where W is O according to the formula of instant claim 1. Berlin teaches compounds of represented by the formula  (DE 19938092, abstract).

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It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the compound taught by Pfleiderer et al. and in view of Haugland et al. with the teaching of Berlin of the compound wherein W is S according to the

formula of instant claim 1. All of Pfleiderer et al., Haugland et al. and Berlin are directed to the field of photolabile protecting groups of nucleosides. One of ordinary skill in the art would be motivated to combine Pfleiderer et al. and in view of Haugland et al. with the teaching of Berlin because Berlin teaches use of the thiocarbonic group results in a protecting group that can be split off very efficiently. One of ordinary skill in the art would have a reasonable expectation of success in combining Pfleiderer et al. and in view of Haugland et al. with the teaching of Berlin because of the structural similarities of the compounds and the teaching of Berlin that said protecting groups can be manufactured analogous to the esters of carbonic acid.

Response to Applicant's Remarks:

Applicant's Remarks, filed 08 Aug 2008, have been fully considered and not found to be persuasive.

Applicant remarks that Berlin teaches a compound that is has different substituents at the aryl ring of the photolabile aryl group. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The disclosure of Pfleiderer et al. of a photolabile phenethyl group combined with the teaching of Haugland et al. of varying the substituents of the photolabile aryl group and further in view of the teaching of Berlin renders obvious the instant invention.

Conclusion

No claim is found to be allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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